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| APPLICATION NO.                                               | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.        | CONFIRMATION NO.       |
|---------------------------------------------------------------|-------------|----------------------|----------------------------|------------------------|
| 10/605,283                                                    | 09/19/2003  | Kapil N. Bhalla      | 1372.76.PRC                | 2282                   |
| 21901                                                         | 7590        | 11/16/2007           |                            |                        |
| SMITH HOPEN, PA<br>180 PINE AVENUE NORTH<br>OLDSMAR, FL 34677 |             |                      | EXAMINER<br>JAGOE, DONNA A |                        |
|                                                               |             |                      | ART UNIT<br>1614           | PAPER NUMBER           |
|                                                               |             |                      | MAIL DATE<br>11/16/2007    | DELIVERY MODE<br>PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/605,283 | <b>Applicant(s)</b><br>BHALLA ET AL. |  |
|                              | <b>Examiner</b><br>Donna Jagoe       | <b>Art Unit</b><br>1614              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 August 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 17-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 17-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                      |                                                                   |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____                                                          | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 21, 2007 has been entered.

***Claims 17-25 are pending in this application.***

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 17 and 18, the phrase "wherein the compound has a concentration between about 1.0 $\mu$ M and about 10.0  $\mu$ M of imatinib mesylate and suberoylanilide hydromaxic acid" renders the claim indefinite because it is unclear whether the amounts recited are equal amounts of each agent or if there is a separate amount of each agent given. Further, it is unclear whether these amounts are measurable before administration, in blood levels, or by some other method.

Claims 17-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Emelen et al. U.S. Patent Application Publication No. U.S. 2005/0096468 A1 with a Provisional priority date of March 13, 2002 taken with Jolivet et al. U.S. Patent No. 6,645,972 with a Provisional Priority date of November 2, 2001.

Van Emelen et al. teach a combination (page 7, paragraph [0114]) of a Histone Deacetylation inhibitor (HDAC inhibitors) (page 6 paragraph [0084]) with another agent to treat cancer and cause apoptosis of cancer cells (page 6, paragraph [0085]) for *inter alia* leukemias (page 6 paragraph [0086]). Agents such as kinase inhibitors, for example imatinib mesylate are recited (page 8 paragraph [0128]) and HDAC inhibitors such as suberoylanilide hydroxamic acid (SAHA) are recited (Page 1, paragraph [0004] and page 8 paragraph [0149]) and a synergistic effect is achieved (page 9, paragraph [0159]). It does not teach exposure of the HDAC inhibitor and the tyrosine kinase inhibitor for about 48 hours, however, Van Emelen et al. teach administration of the agents "once, twice or more per course of treatment, which may be repeated, for example every 7, 14, 21 or 28 days. If the agent is administered daily, this would encompass exposure for about 48 hours (page 9, paragraph [0170]). It would have been obvious to employ the HDAC inhibitor and the tyrosine kinase inhibitor for about 48 hours motivated by the teaching of Van Emelen et al. that the HDAC inhibitors along with another chemotherapeutic agent, such as kinase inhibitors, for example imatinib mesylate are recited (page 8 paragraph [0128]) can be administered once, twice or more per course of treatment, which may be repeated, for example every 7, 14, 21 or

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28 days. It does not teach the method where the cancer cells are imatinib mesylate refractory. Jolivet et al. teach treatment of acute leukemia is very complex (column 1, line 35) and resistance to agents occurs, particularly in Bcr-Abl tyrosine kinase inhibitor (column 3, lines 25-60) such as imatinib mesylate (column 2, lines 39-51). Van Emelen teach a synergistic effect when another medicinal agent and HDAC inhibitor are administered simultaneously or sequentially (page 9, paragraph [0159]). It is noted that there are other agents recited for treatment of cancer/leukemia. The claim language *comprising* leaves the claim open for the inclusion of unspecified ingredients, even in major amounts. It would have been obvious to one of ordinary skill in art at the time it was made to employ inhibitors of HDAC along with Bcr-Abl tyrosine kinase inhibitors to induce apoptosis in leukemia, as taught by Van Emelen et al. especially where there is resistance to the Bcr-Abl tyrosine kinase inhibitors, normally employed to treat leukemia and taught by Jolivet et al.

### ***Response to Arguments***

Applicant asserts that the provisional application of Van Emelen et al. has not been provided to applicant.

In June 2004, the USPTO ceased mailing paper copies of cited U.S. patents and U.S. patent application publications with all Office actions. See "USPTO to Provide Electronic Access to Cited U.S. Patent References with Office Actions and Cease Supplying Paper Copies," 1282 O.G. 109 (May 18, 2004). Foreign patent documents and non-patent literature will continue to be provided to the applicant on paper.

All U.S. patents and U.S. patent application publications are available free of charge from the USPTO web site ([www.uspto.gov/patft/index.html](http://www.uspto.gov/patft/index.html)), for a fee from the Office of Public Records (<http://ebiz1.uspto.gov/oems25p/index.html>), and from

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commercial sources. Copies are also available at the Patent and Trademark Depository Libraries (PTDLs). A list of the PTDLs may be found on the USPTO web site ([www.uspto.gov/web/offices/ac/ido/ptdl/ptdlib\\_1.html](http://www.uspto.gov/web/offices/ac/ido/ptdl/ptdlib_1.html)). Additionally, a new feature in the Office's Private Patent Application Information Retrieval system (PAIR), E-Patent Reference, is available for downloading and printing of U.S. patents and U.S. patent application publications cited in U.S. Office Actions.

## **STEPS TO USE THE E-PATENT REFERENCE FEATURE**

Access to Private PAIR is required to utilize E-Patent Reference. If you do not already have access to Private PAIR, the Office urges practitioners and applicants not represented by a practitioner to: (1) obtain a no-cost USPTO Public Key Infrastructure (PKI) digital certificate; (2) obtain a USPTO customer number; (3) associate all of their pending and new application filings with their customer number; (4) install free software (supplied by the Office) required to access Private PAIR and the E-Patent Reference; and (5) make appropriate arrangements for Internet access.

### **Instructions for performing the 5 steps:**

**Step 1:** Full instructions for obtaining a PKI digital certificate are available at the Office's Electronic Business Center (EBC) web page ([www.uspto.gov/ebc/downloads.html](http://www.uspto.gov/ebc/downloads.html)). Note that a notarized signature will be required to obtain a digital certificate.

**Step 2:** To get a Customer Number, download and complete the Customer Number Request form, PTO-SB/125, from the USPTO web site ([www.uspto.gov/web/forms/sb0125.pdf](http://www.uspto.gov/web/forms/sb0125.pdf)). The completed form can be transmitted by facsimile to the Patent Electronic Business Center at (571) 273-0177, or mailed to the address on the form. If you are a registered attorney or agent, your registration number must be associated with your customer number. This association is accomplished by adding your registration number to the Customer Number Request form.

**Step 3:** A description of associating a customer number with the correspondence address of an application is described at the EBC Web page ([www.uspto.gov/ebc/registration\\_pair.html](http://www.uspto.gov/ebc/registration_pair.html)).

**Step 4:** The software for electronic filing is available for downloading at [www.uspto.gov/ebc](http://www.uspto.gov/ebc). Users can also contact the EFS Help Desk at (571) 272-4100 and request a copy of the software on compact disc. Users will also need Adobe Acrobat Reader, which is available through a link from the USPTO web site.

**Step 5:** Internet access will be required which applicants may obtain through a supplier of their own choice. As images of large documents must be downloaded, high-speed Internet access is recommended.



The E-Patent Reference feature is accessed using a button on the Private PAIR screen. Ordinarily all of the cited U.S. patent and U.S. patent application publication references will be available over the Internet using the Office's new E-Patent Reference feature. The size of the references to be downloaded will be displayed by E-Patent Reference so the download time can be estimated. Applicants and registered practitioners can select to download all of the references or any combination of cited references. Selected references will be downloaded as complete documents in Portable Document Format (PDF). The downloaded documents can be viewed and printed using commercially available software, such as ADOBE® READER®. ADOBE® READER® is available free of charge from Adobe Systems Incorporated ([www.adobe.com/products/acrobat/readermain.html](http://www.adobe.com/products/acrobat/readermain.html)).

In response to Applicants' assertion that Van Emelen et al. is only entitled to the PCT filing date of March 11, 2003, 35 U.S.C. 102(e) is explicitly limited to certain references "filed in the United States before the invention thereof by the applicant" (emphasis added). The PCT filed by Van Emelen et al. was filed in Europe.

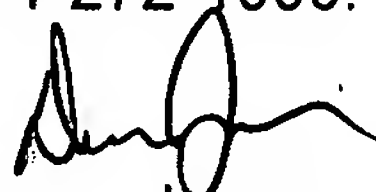
### ***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Donna Jagoe  
Patent Examiner  
Art Unit 1614

November 10, 2007